

CLAIMS

What is claimed is:

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1. A method for obtaining *in vivo* binding partners of a protein of interest in a cell type, the method comprising:

- (a) obtaining a cell of said cell type transformed to express a fusion protein, said fusion protein comprising:
- 10 (i) said protein of interest; and
- (ii) a post-translational modification sequence;
- (b) growing said cell or progeny of said cell under conditions which permit expression and post-translation modification of said fusion protein to produce a tagged fusion protein;
- 15 (c) contacting an extract of said cell or progeny of said cell with an affinity purification reagent which specifically binds to said tagged fusion protein to form a complex; and
- (d) separating said complex from said extract.

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2. The method of claim 1, wherein an enzyme that performs the post-translation modification of said fusion protein is not naturally expressed in the cell of said cell type, and is encoded by a vector which is introduced into the cell.

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3. The method of claim 1, wherein the cell is a mammalian cell.

4. The method of claim 1, further comprising identifying any binding partners of said protein of interest in said complexes.

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5. The method of claim 1, wherein said fusion protein further comprises an affinity purification sequence selected from the group consisting of polyhistidine, *S. aureus* protein A IgG binding domain, glutathione-S-transferase binding domain, maltose binding protein, cellulose binding domain, calmodulin binding peptide, an epitope tag, and combinations thereof.

6. The method of claim 1, wherein said fusion protein further comprises a cleavage site between said protein of interest and said post-translational modification sequence, and said method further comprises the steps of:

- 5 (a) cleaving said cleavage site after separating said complex from said extract to form a cleaved protein of interest; and
- (b) separating said cleaved protein of interest from said post-translational modification sequence prior to identifying any binding partners of said protein of interest.

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7. The method of claim 1, wherein the protein of interest further comprises an affinity purification sequence selected from the group consisting of polyhistidine, *S. aureus* protein A IgG binding domain, glutathione-S-transferase binding domain, maltose binding protein, cellulose binding domain, calmodulin binding peptide, an epitope tag, and combinations thereof, and wherein the affinity purification sequence remains attached to the protein of interest after cleaving said cleavage site.

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8. The method of claim 7, further comprising affinity purifying the protein of interest after the separating step.

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9. A method for obtaining *in vivo* binding partners of a protein of interest in a cell type comprising:

- (a) transforming a cell of said cell type with a vector encoding a fusion protein, the fusion protein comprising:
 - 25 (i) said protein of interest;
 - (ii) a post-translational modification sequence;
- (b) growing said cell or progeny of said cell under conditions which permit expression and post-translation modification of said fusion protein to produce a tagged fusion protein;
- 30 (c) contacting an extract of said cell or progeny of said cell with an affinity purification reagent which specifically binds to said tagged fusion protein to form a complex; and
- (d) separating said complex from said extract.

10. The method of claim 9, wherein the cell is a mammalian cell.

11. The method of claim 9, further comprising identifying any binding
5 partners of said protein of interest in said complexes.

12. The method of claim 9, wherein said fusion protein further comprises an
affinity purification sequence selected from the group consisting of polyhistidine, *S.*
aureus protein A IgG binding domain, glutathione-S-transferase binding domain,
10 maltose binding protein, cellulose binding domain, calmodulin binding peptide, an
epitope tag, and combinations thereof.

13. The method of claim 9, wherein said fusion protein further comprises a
cleavage site between said protein of interest and said post-translational modification
15 sequence, and said method further comprises the steps of:

- (a) cleaving said cleavage site after separating said complex from said
extract to form a cleaved protein of interest; and
- (b) separating said cleaved protein of interest from said post-translational
20 modification sequence prior to identifying any binding partners of said
protein of interest.

14. The method of claim 9, wherein the protein of interest further comprises
an affinity purification sequence selected from the group consisting of polyhistidine,
S. aureus protein A IgG binding domain, glutathione-S-transferase binding domain,
25 maltose binding protein, cellulose binding domain, calmodulin binding peptide, an
epitope tag, and combinations thereof, and wherein the affinity purification sequence
remains attached to the protein of interest after cleaving said cleavage site.

15. The method of claim 14, further comprising affinity purifying the protein
30 of interest after the separating step.

16. A method for screening a plurality of potential binding partners for
binding to a protein of interest, the method comprising:

- (a) obtaining a cell transformed to express a fusion protein, said fusion protein comprising:
 - (i) said protein of interest; and
 - (ii) a post-translational modification sequence;
- 5 (b) growing said cell or progeny of said cell under conditions which permit expression and post-translation modification of said fusion protein to produce a tagged fusion protein;
- (c) introducing into the cell the plurality of potential binding partners;
- (d) contacting an extract of said cell or progeny of said cell with an
10 affinity purification reagent which specifically binds to said tagged fusion protein to form a complex; and
- (e) separating said complex from said extract.

15 17. The method of claim 16, wherein the plurality of potential binding partners are encoded by a plurality of nucleic acid expression vectors that when introduced into the cell result in the expression in the cell of the plurality of potential binding partners.

20 18. An expression vector encoding a fusion protein, wherein the fusion protein comprises a protein of interest and a post-translational modification sequence.

19. A cell comprising the expression vector of claim 18.